tion of the ear—the affection of the cochlear branch of the 8th nerve where the vestibular branch is not affected, or the affection of the vestibular branch where the cochlear is not affected.

In all nerve lesions in congenital lues we find the adequate function disappears first and the inadequate function later. The turning nystagmus will disappear first, and we have non-reaction to the turning motion and still reaction to the caloric. The normal function disappears, but we can still stimulate that nerve by electricity or cold water.

Dr. E. D. Chipman: I can not quite allow the impression Dr. Graham has given concerning fissures of the tongue. The smooth atrophy on the back of the tongue is very significant of lues, but you will often find a fissure of the tongue, and a congenitally grooved tongue when there is no sign of syphilis.

Concerning the transitory and scattered flush areas, while these fugacious erythemas do occur in excitable people, many of the people who are excitable and blush easily are not luetic. It would not be safe to consider this manifestation as significant.

GASTRO-INTESTINAL SYMPTOMS IN DISEASES OF THE CIRCULATORY SYSTEM.

By DR. WILLIAM WATT KERR, San Francisco.

The relation between gastro-intestinal disorders and affections of the circulatory system is not infrequently overlooked, yet disturbed alimentation may be the only indication of weakened myocardium in elderly people or others who are not subjected to sufficient exertion to awake dyspnea, but whose poor circulation leads to portal congestion with its attendant dyspepsia and even more grave consequences.

It is easy to understand that an incompetent mitral valve may result in failure of the tricuspid valve and myocardium, together with portal obstruction and passive congestion of the liver, pancreas, stomach and intestines, so that the function of all these organs is seriously impaired; but there is another group of cases from which edema and valvular murmurs may be entirely absent, where the trouble lies in changes that have taken place in the blood vessels and cardiac muscle as part of the ordinary senile degeneration, or in consequence of disease or dietetic excesses, and these are not so readily recognized.

It must be remembered that the mesenteric vessels are a very common seat of arterio-sclerosis, in fact possibly only the aortic and coronary arteries show a greater susceptibility; and this being the case, it is easy to understand that the organs supplied by these diseased vessels are liable to undergo changes consequent upon their malnutrition, and possibly in some instances as a local effect of the toxins that caused the sclerosis. It is not, therefore, a matter of surprise that such changes as cellular atrophy and degeneration, fibrosis, and even ulceration, should have been found in the affected viscera. The symptoms necessarily vary with the organs whose functions are chiefly involved. The gastric symptoms may be those of chronic flatulent dyspepsia with occasional nausea and vomiting, or those of gastric ulcer, indeed ulceration may be present, so that sometimes it is difficult to decide whether hematemesis is due to vascular erosion or to diapedesis.

Occasionally these milder conditions are supplemented at intervals of one or more days by paroxysmal seizures of gastric pain and distension which may be relieved by belching and vomiting, while in other instances marked dyspnea is present and the abdominal pain is so great that in all probability they are cases of abdominal angina due to spasm of the splanchnic arterioles, a condition to which the smaller sclerosed vessels are particularly prone. Cases of such severity, however, are not very common, or it may be that they are not recognized because the superficial vessels do not happen to be markedly involved.

It must never be forgotten that a comparative healthy condition of the radial and temporal vessels does not by any means warrant the conclusion that the aorta, coronary and mesenteric arteries are likewise free from sclerosis.

The type of cases to which at this time particular reference is made are those where the patient is free from all gastric discomfort with the exception of an occasional feeling of nausea and retching that may be accompanied by faintness and vertigo; or such attacks may occur as exacerbations in the sickness of a patient who continuously suffers from anorexia and nausea. The condition is due to disturbances in the cerebral circulation, and is most frequent in old people.

The following histories will probably serve for purposes of illustration:

(1) A man eighty-six years old, but of active habits, was awakened suddenly during the night by a desire to urinate. Immediately after emptying his bladder he was affected with "a horrible feeling of nausea and faintness, with a desire to vomit." He was given a cup of hot water by one of his family in the hope that it would cause him to vomit, and thus allay the violence of the retching, but he retained it, dropped into a sound sleep, and awoke the next morning none the worse for his experience. Although this man has a considerable degree of sclerosis, yet his heart and blood vessels are in exceptionally good condition for one of his years, so that he is still engaged in active business pursuits. Neither is he subject to any gastro-intestinal discomfort, but has a good appetite, good digestion, and is careful with regard to his diet. The nausea without doubt was due to disturbance of the cerebral circulation in consequence of the sudden assumption of the upright position after being recumbent for so many hours, and was contributed to by the emptying of a distended bladder lowering the blood pressure.

In the foregoing instance, the etiology of the nausea was to a very great extent mechancial in character, but in the following case arterial spasm was the prominent factor.

(2) A lady, seventy-one years old, when traveling in Europe and subjected to considerable fatigue and anxiety, exhibited symptoms of cerebral disturbance for some hours, that were believed to be the result of slight cerebral edema. For several years after this she remained in good health, but had to be careful in her diet on account of dyspepsia. One evening while quietly reading she had a sensation of chilliness and nausea that lasted for a few minutes and then passed away so completely that half an hour later she laughingly

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said that she was all right, and probably had been unnecessarily alarmed, but that the sensation while it lasted was "very queer."

Examination failed to reveal anything different from her usual condition, but in compliance with her own request she was allowed to take two grains of calomel. During the next few days she appeared to be in her usual health, but on the evening of the seventh day she had a similar, yet more serious attack, the latter part of which I witnessed.

Like the former, it began with chilliness, nausea and a sensation of oppression over the sternum, and after repeated retching she brought up about two drachms of food that she had swallowed half an hour previously; the pulse became very small, the patient lost consciousness for a few minutes but recovered quickly after an injection of caffeine, so that two hours later she expressed herself as being in her usual health.

Six days afterwards, during an examination of the patient, I noticed that the pulse suddenly became small from contraction of the artery, not from emptiness; simultaneously she yawned repeatedly, shivered, and complained of chilliness, nausea, and oppression over the sternum that rapidly increased to pain. Caffeine and nitroglycerine were at once injected, and soon the radial artery began to relax and the shivering to diminish, but, after an interval of ten minutes, as she still complained of nausea and sternal pain, two drops of spirit of glonoin were placed on her tongue, and this was followed by a general relaxation of all the blood vessels and disappearance of the symptoms.

At this time she spoke quite distinctly, and expressed herself as feeling comfortable, although very much exhausted; but about twenty minutes later it was noticed that her speech had become somewhat thick, and that she had slight difficulty in swallowing.

These symptoms had entirely disappeared by the next morning—probably from absorption of edema.

The nurse told me that on two or three occasions during the preceding week she had complained of nausea, chilliness and praecordial pressure, but had been relieved at once by the administration of caffeine and nitro-glycerine.

In this patient the somatic vessels do not show any marked degree of sclerosis, but it is possible that the splanchnic area is not equally good, as although she never has any acute attacks of indigestion, she always requires some aid to digestion even when following a careful dietary.

Conflicting opinions of physiologists regarding the regulation of the cerebral circulation makes it difficult to interpret the above symptoms. The repeated yawning, so strongly indicative of cerebral anemia, might be explained by the extension of the general arterial contraction to the cerebral vessels. But the more popular physiological belief is that the cerebral arterioles are destitute of vaso-motor fibers, and that the circulation through the brain is regulated by variations in aortic pressure.

This leaves us one of two alternatives; either the contraction of the carotids and vertebrals before they reach the circle of Willis, when vaso-motor control appears to cease, was so intense that an adequate circulation could not be maintained through the sclerosed cerebral arteries; or, what is more in conformity with accepted physiological views, owing to the diseased condition of the entire vascular system the mechanism for maintaining the ordinary physiological relations between intracranial and general arterial pressure was disturbed, so that an extensive spasmodic contraction in the latter areas, which is not uncommon in general arteriosclerosis, was followed by an increased intracranial pressure and a secondary anemia of the centers in the medulla, causing the sensation of nausea and the desire to yawn.

The distinctly perceptible contraction of the radial artery with the simultaneous production of shivering and precordial oppression, rapidly developing into the pain of angina pectoris, all suggested an extensive arterial contraction, both somatic and splanchnic, with consequent rise in aortic pressure and sudden increase in the volume of blood flowing into the less resisting cerebral vessels.

In searching for the etiology of the attack it has been impossible to discover any exciting cause beyond the established fact that the arterioles in sclerosed vessels are particularly prone to spasm.

Enough has been said to emphasize the importance of attempting to discover the particular cause of the nausea in each case, instead of indiscriminately prescribing bismuth, laxatives, or some similar routine treatment. These, without doubt, are most useful adjuvants in cases of passive congestion of the various alimentary organs consequent upon failing compensation, but their sphere is decidedly limited where there is any marked degree of arteriosclerosis.

I do not know of anything more distressing both to patient and physician than the persistent nausea and absolute horror of food that frequently exists in cases of advanced senile cardio-vascular disease.

Here the endeavor should be to restore the balance between the splanchnic and somatic vascular areas that has been upset by the sclerotic process. As the splanchnic area is the one which normally plays the greater part in the adjustment, it is probable that alimentary disturbance indicates an extensive involvement of the arteries supplying the viscera, and this is borne out by the surprising frequency with which we see extensive sclerosis of the superficial vessels without the production of any special symptoms. I have advisedly used the expression "Maintain the balance" because the nausea may be the result of excessive lowering, excessive raising, or irregularities of the blood supply to the brain, and consequently it is sometimes a matter of difficulty to adjust the treatment to the requirements of the individual case.

It might facilitate matters if, for purposes of treatment, each of these cases of nausea was regarded as belonging to one of four groups. (1) Those cases where the nausea is essentially the result of passive portal congestion. (2) Those in which it is mainly due to sclerosis in the mesenteric vessels. (3) Those in which the attacks are only occasional, are cerebral in origin, and consequent upon arteriosclerosis producing irregularities in the blood supply to the brain. (4) Those in which two or more of the above conditions are combined.

In the first group the treatment is based upon the lines usually followed in restoring ruptured compensation; mercurials and laxatives to relieve the congestion, combined with some member of the digitalis group to restore compensation, and possibly during convalescence it may be advisable to ad-

minister hydrochloric acid and nux vomica for the purpose of aiding digestion and giving tone to the stomach.

The second group is not infrequently associated with the production of sternal pain if the patient exerts himself soon after eating. The ingestion of food is normally followed by dilatation of the splanchnic area and an increased flow of blood through the digestive organs whose function is called into play; but the thickening of the sclerosed vessels, together with their increased tendency to spasm, interferes with this necessary augmentation of the blood supply; consequently various degrees of indigestion and nausea ensue.

The best results from treatment are obtained when the diet is regulated by reducing the size of the meals, giving easily digested foods, and limiting as far as possible the consumption of proteids.

The medication consists in regulating the bowels, so that the patient has at least one daily evacuation, and in addition to this, every fifth or sixth day, especially if the patient be plethoric, a mild catharsis should be produced by such agencies as Hunyadi or Apenta water, or any salines of similar character. This may be all that is required, but some cases demand further medication, and at such times theobromine sodium salicylate has been found to yield most excellent results.

This remedy has a selective action for the splanchnic area, and appears to act directly upon the vessels rather than upon the nerve centers. It relieves the vascular spasm, dilates such sclerosed vessels as are still capable of responding to its stimulus, and thus ensures a better blood supply to the different viscera and a consequent increased capability for their functional activity.

Of course, failure may take place from various causes, such as the sclerosis in certain vessels being so far advanced that they are no longer responsive, but it is also possible that the viscus itself has undergone degenerative changes as a result not only of the prolonged sclerosis, but also because the same agents that injured the vessels may have simultaneously exercised a destructive influence on the cells of the viscus. The best results are obtained when the remedy is given fully half an hour before food, as absorption takes place more readily under such conditions, and the blood supply to the stomach in this way anticipates the food that is to be ingested. Five grains is generally a sufficient dose, and in many instances it has to be given only before the heaviest meal.

Where theobromine has failed to give relief I have used the extract of thyroid gland with decided benefit, so that not infrequently the theobromine is used for two or three weeks, and after an interval of a few days the thyroid extract has been substituted for a like period, the two remedies being alternated from time to time with intervals varying in length with the condition of the patient. It appears to be most valuable in those cases of nausea associated with a persistently high blood pressure that do not yield to a strict dietetic and hygienic treatment.

Formerly I combined the thyroid with caffeine to counteract the supposed tendency to cardiac depression, but since Oliver and Schafer ("Regulators of Metabolism," by Noel Paton, page 83, Macmillan and Co., 1913) showed that there is no such action, and that the fall of arterial pressure is simply the result of dilatation of the arterioles, I no longer do so unless some co-existing condition of the heart demands stimulation.

Another advantage possessed by thyroid lies in the fact that it is a sensitizer of nerves influencing the circulation. During the administration of remedies that act upon the vasomotor system one must face the thought that while one result on the splanchnic area, such as dilatation of the blood vessels, may be desirable at some particular stage of digestion or in some organ, it may be that the opposite (a state of constriction) is necessary at some other stage or in some other viscus that is simultaneously in a state of activity, and consequently that the remedy, by a prolonged effect or by an influence antagonistic to the requirements of some other organ, may ultimately do more harm than good.

It is not probable that this objection can be urged universally against the use of thyroid because Asher and Von Rodt state "that thyroid extracts sensitize the nerve terminations upon which adrenalin acts. Upon stimulating the splanchnic nerve the usual vaso-constriction and rise of blood pressure becomes more marked after the administration of thyroid preparations." (Noel Paton, as above.)

As arteriosclerosis is not infrequently found in patients suffering from exophthalmic goitre, it is not likely that thyroid extract has any direct influence upon metabolism that will prevent sclerosis. The dose of thyroid extract varies in different cases, the average being three grains from one to three times daily.

The third group in which the nausea is dependent upon irregularities in the cerebral circulation, requires consideration of the blood pressure and also of the heart before selecting the remedy.

When the general blood pressure is high the best results are apparently obtained from theobromine sodium salicylate, in doses of from five to seven grains three times daily, but if the heart be weak and the pressure about normal or lower, better results are obtained from a combination of small doses of nitroglycerine and caffeine sodium benzoate, with the addition of ten grains of strontium bromide to each dose, for the purpose of allaying the cerebral excitement that caffeine is apt to produce.

Small doses of digitalis may be substituted for the caffeine in this combination, but the latter is more prompt in its action than digitalis and much better adapted for hypodermatic medication.

The fourth group, where we have a combination of circulatory disturbances, is particularly common in old people, because it is in those that sclerosis is best marked, and in addition there are generally senile changes in the myocardium which impair the blood supply to the brain and other organs.

Such cases necessitate a careful scrutiny to detect the preponderating factors, and a combination of

the various forms of treatment already mentioned in proportion to the varying individual demands.

No matter how hard one tries to remove this subjective sensation of nausea, it often happens that all those methods fail. Then all that can be done is to diminish the sensibility of the nerve center, a result which is best attained by the administration of morphine in small doses, one-sixteenth to one-eighth of a grain three or four times daily.

Without doubt it is the beginning of the end, but when the narcotic is given in the smallest effective doses, and in combination with other remedies, it very frequently prolongs life and converts an existence of inactivity and suffering into one of comparative usefulness and comfort.

BENZENE TREATMENT OF LEUKEMIA.*

By W. W. BOARDMAN, M.D., San Francisco.

Of the etiology of the leukemias, we know nothing. The essential morbid process is an excessive and abnormal activity of the leukoblastic tissues of the body, manifested by an increase in the number and an alteration in the character of the circulating leukocytes. A specific remedy would destroy the unknown exciting factor, be it toxic, infectious or what not. Lacking this, our therapeutic efforts are limited to attempts to control the excessive activity of the leukoblastic tissues. For this purpose, arsenic has for years been used; more recently the X-ray, radium and thorium x have been added. With each and all of these measures, striking improvements may occur but with none do permanent cures result. New hopes were therefore raised by Koranyi's[28] report in 1912 of the striking effect obtained with benzol.

Benzol is the loose trade name applied to one of the early distillation products of coal tar, consisting largely of benzene with small amounts of toluene, xylene, carbon disulphid, pentone, thiophane, water and traces of impurities. The name is also incorrectly applied to benzene, a definite chemical compound C_6H_6. Benzol is used industrially as a solvent and several cases of poisoning have occurred among those exposed to its action.

Santesson,[47] in 1897, reported a series of cases of chronic poisoning occurring among the employees of a bicycle tire plant. Four of these cases died. He produced chronic poisoning in rabbits, a characteristic finding being the marked hypoplasia of the bone marrow. Other cases of industrial poisoning have been reported by Gerbis,[17] Beisele,[4] and Schultz.[51]

Selling,[52] in 1910, studied four cases of chronic poisoning occurring in Baltimore, two of which came to autopsy. He concluded from this, and from his animal experiments that benzene C_6H_6 is the active poison in commercial benzol; that the signs of chronic poisoning are giddiness, headache, gastro-intestinal disturbances, pupura and anemia; that the characteristic blood changes are a marked leukopenia with decrease in the granular type of white cell, with relative increase in the mononuclear elements, decrease in the number of platelets, decrease in the amount of hemoglobin and in the number of erythrocytes and an absence of regenerative forms; and finally, that the constant anatomical finding is a marked hypoplasia of the bone marrow. It was therefore evident that in benzene we possessed a substance capable of producing marked hypoplasia of normal bone marrow with a blood picture resembling (except for the more marked leukopenia) an aplastic anemia.

With this action of benzol in mind, Von Koranyi[28] applied it in the treatment of six cases of leukemia. With it he obtained marked subjective improvement, decrease in the size of the spleen and lymph glands, increase in the number of red cells, increase in the amount of hemoglobin and a decrease in the number of leukocytes to normal or practically normal values. There was however a persistence, though in a lessened degree, of the abnormal qualitative findings. Case reports have rapidly multiplied so that at present there are more than one hundred on record. A striking unanimity of opinion exists among these authors regarding the efficacy of benzene. Sixteen out of one hundred failed to show improvement. Another eight cases, although reacting favorably at first, died during or soon after the discontinuance of the treatment. Seventy-five cases, or 75%, showed improvement during the period of observation. Any measure producing improvement in 75% of a large series of patients treated in widely separated sections demands our serious consideration.

In such a consideration there are certain questions to be answered. 1. Is the principle of the treatment sound? 2. Is there any danger in the treatment? 3. Is the improvement real or only apparent? 4. Is the improvement lasting? 5. Is the treatment applicable in all cases? 6. What are the advantages of the treatment over other methods? 7. And finally, what is the best method of applying the treatment?

As has been stated, the essential morbid process in leukemia is an excessive and abnormal activity of the leukoblastic tissues. Our problem is to control this excessive activity. We now have abundant experimental and clinical proof that benzene acts upon the leukoblastic tissues, causing a marked decrease in their functional activity in both normal and abnormal states. This is evidenced in the investigation of the cases of industrial poisoning by Santessan, Selling and others, in the experimental work of Santessan, Selling, Pappenheim and others, from the study of several cases of leukemia dying with an aplastic bone marrow from over dosage, and finally by the many successful clinical cases. Therefore, as Koranyi concluded, benzene meets this first requirement.

A second and more important requirement is that benzene, in exerting its effect on the leukoblastic tissues, shall in no way seriously injure the body as a whole or any of the individual tissues. Reports show the occurrence, during the administration of benzene, of gastro-intestinal disturbances, headaches, dizziness, skin eruptions, bronchial irritation, kidney irritation, marked leukopenia, hemorrhages, increasing anemia and death. The cases of industrial poisoning confirm these

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